Version
2.1.2.0

Abstract

Grant Number: 1 X01MH78942-01

PI Name: PELLECCHIA, MAURIZIO

PI Email: MPELLECCHIA@BURNHAM.ORG

Project Title: Chemical Tools to Investigate the Protein Folding/Degradation Machinery

Abstract: *DESCRIPTION (provided by applicant):* The misregulation of protein folding quality control and protein degradation often results in a variety of deleterious consequences on cellular function that range from the accumulation of non-native protein species or protein aggregates leading to neurological disorders, to the inhibition of apoptosis in cancer cells. Several components of the protein folding/degradation machinery have been identified and characterized. A large body of evidence suggests that the regulation of the protein folding/degradation machinery represents a viable target for the development of novel potential therapies against several human malignancies. However, further research in this area is hampered by the lack of effective pharmacological tools. To this end, we propose an innovative approach aimed at the identification of small molecule probes capable of modulating the activity of the chaperone Hsp70 by targeting its substrate binding-domain. Such probe-ligands would open the way to a plethora of experiments with human cancer cells to dissect the multitude of activities that have been attributed to the chaperone in the onset and progression of cancer and ultimately may provide a framework onto which to develop potentially novel anti-cancer therapies. Two other possible targets are also discussed that are involved in the early stages of protein folding and degradation.

Thesaurus Terms: protein folding, protein degradation, small molecule probes, probe-ligands, chaperone Hsp70, anti-cancer therapies, cancer cells

Institution: BURNHAM INSTITUTE
10901 NORTH TORREY PINES ROAD
LA JOLLA, CA 92037

Fiscal Year: 2007

Department:	CANCER RESEARCH CENTER
Project Start:	2006/07/25
Project End:	2007/07/25
ICD:	NATIONAL INSTITUTE OF MENTAL HEALTH
IRG:	ZMH1